



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2014-N-2187]

Identifying Potential Biomarkers for Qualification and Describing Contexts of Use to Address Areas Important to Drug Development; Request for Comments

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice; request for comments.

SUMMARY: The Food and Drug Administration (FDA or Agency) is seeking information to facilitate development and qualification of biomarkers in areas related to human drug therapeutics. Towards this goal, FDA is encouraging interested groups and individuals to submit information on specific medical and biological areas where novel biomarkers can be identified that would meaningfully advance drug development. FDA encourages respondents to describe evidentiary considerations that are important to qualify these biomarkers for a specific context of use. Details of information that should be provided to the Agency are described in the survey.

DATES: Submit either electronic or written comments by [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER].

ADDRESSES: You may submit comments by any of the following methods:

Electronic Submissions

Submit electronic comments in either of the following ways:

- Federal eRulemaking Portal: <http://www.regulations.gov>. Follow the instructions for submitting comments.

- SurveyMonkey Link: <https://www.surveymonkey.com/s/RHJLHS7>. This survey may be used to provide feedback on answers to questions regarding potential biomarkers for qualification and to describe contexts of use to address areas important to drug development.

Written Submissions

Submit written submissions in the following ways:

- Mail/Hand delivery/Courier (for paper submissions): Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

Instructions: All submissions received must include the Docket No. FDA-2014-N-2187 for this document. All comments received may be posted without change to <http://www.regulations.gov>, including any personal information provided. It is only necessary to send one set of comments. For additional information on submitting comments, see the “Request for Information” heading of the SUPPLEMENTARY INFORMATION section of this document.

Docket: For access to the docket to read background documents or comments received, go to <http://www.regulations.gov> and insert the docket number, found in brackets in the heading of this document, into the “Search” box and follow the prompts and/or go to the Division of Dockets Management, 5630 Fishers Lane, rm.1061, Rockville, MD 20852, between 9 a.m. and 4 p.m., Monday through Friday.

FOR FURTHER INFORMATION CONTACT: Marianne Noone, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 21, rm. 4528, Silver Spring, MD 20993-0002, 301-796-7495.

SUPPLEMENTARY INFORMATION:

I. Background

The President signed into law the Food and Drug Administration Safety and Innovation Act (FDASIA) (Public Law 112-144) on July 9, 2012. Title I of FDASIA reauthorizes the Prescription Drug User Fee Act (PDUFA) and provides FDA with the user fee resources necessary to maintain an efficient review process for human drug and biological products. The reauthorization of PDUFA added performance goals and procedures for the Agency that represent FDA's commitments during fiscal years 2013 through 2017. These commitments are fully described in the document entitled "PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2013 through 2017" (PDUFA Goals Letter), available on FDA's Web site at

<http://www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM270412.pdf>

f. Section IX of the PDUFA Goals Letter entitled "Enhancing Regulatory Science and Expediting Drug Development" references support for the identification and advancement of biomarkers.

A biomarker is an objective characteristic that is measured and evaluated as an indicator of normal biologic processes, pathogenic processes, or pharmacologic responses to treatment. Biomarkers can serve many purposes in clinical drug development, including the following: Defining the appropriate patient populations for study, as well as those who should receive the drug in clinical practice; pharmacodynamic markers for proof of concept and dose selection; and pharmacodynamic markers of adverse effects. A subset of pharmacodynamic biomarkers can serve as replacements for clinical efficacy endpoints that reflect how a patient feels, functions, or survives. The path to development of promising therapeutics can be enabled by the availability of biomarkers that are analytically validated and clinically qualified for a specific context of use

(i.e., a comprehensive, clear, and precise statement that describes the manner of use, interpretation, and purpose of use of a biomarker in drug development).

Qualification is based on a body of evidence that demonstrates that the biomarkers are fit for purpose in drug development and evaluation

(<http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DrugDevelopmentToolsQualificationProgram/ucm284076.htm>). Further, qualification is dependent on the specific proposed context of use. Biomarkers that are qualified can help to progressively reduce uncertainty about the outcome of clinical development programs.

Public/private partnerships involving regulatory, academic, and industry scientists, collaborating within a precompetitive framework, are essential to catalyzing progress. Because of limitations in resources, such efforts must be focused on the opportunities that offer the greatest potential for impact.

FDA intends to facilitate identification of the most promising biomarkers and the areas important to drug development and to promote efforts that will aid in the qualification and regulatory adoption of the drug development framework.

II. Request for Information

FDA is seeking public feedback to identify promising biomarker candidates in areas important to drug development and to identify considerations for evidence needed to qualify various types of biomarkers for specific contexts of use. FDA requests identification of specific biomarkers with a proposed context of use and of the type of evidence needed to support qualification. After reviewing the information provided, FDA will post the collated information on its Web site.

A. Information Requirements

In general, submitted information should include the following for each biomarker nominated, as well as any other relevant information:

- Areas that have a critical need for biomarkers to assist drug development;
- The name of the biomarker;
- The proposed context of use for the biomarker (if known);
- The reason why the biomarker should be considered, taking into account its usefulness as a drug development tool; and
- Any evidence that should be developed to support qualification of the biomarker.

B. Questions and Requests

Specific questions and requests are as follows:

1. Are there specific aspects of drug development that could be enhanced through the development of biomarkers?

a. Please list the specific applications of biomarkers that address areas important to drug development.

b. Please list the specific areas (for example, a specific disease area or an organ toxicity) needed for development of biomarkers important to drug development.

c. Is there information or efforts which could be leveraged to advance these areas? If yes, please describe.

d. Are there areas that appear to be promising for the development of new biomarkers and for which collaborative engagement from stakeholders offers a path forward? If so, please explain.

- Are there groups positioned to accomplish this? If yes, please describe.

e. Are there barriers that preclude engagement or investment in biomarkers for these priority areas? If yes, please explain.

2. In each of these priority areas that are important to drug development, please provide the following information:

a. Biomarker: What specific biomarkers do you believe represent the greatest near-term opportunity to establish utility in drug development (i.e., that could be substantially advanced by facilitating discussion and consensus building)?

b. Rationale: Why should the biomarker(s) be included on the list, taking into account its usefulness in regulatory decisionmaking as a drug development tool?

c. Context of use: Can you please describe/propose a specific context of use for the biomarker(s)?

d. Evidentiary gaps: To support the proposed context of use, what do you see as the largest evidentiary gaps that need to be addressed to permit “fit for purpose” qualification?

e. How can these evidentiary gaps be addressed?

f. Collaborative data sharing: Can any of these gaps be addressed by collaborative data sharing of existing data versus prospective studies specifically dedicated to addressing the gap?

3. Please indicate your affiliation from the following list: academia, pharmaceutical sector, biotechnology sector, government, professional organization, non-profit organization, clinician, patient advocacy group, patient, or other (please provide specifics, if you choose other).

III. Paperwork Reduction Act

This Federal Register notice requests input from biomarker experts from academia, the pharmaceutical industry, and government organizations on the evidentiary standards for biomarkers or on the expectations about data for qualification of different types of biomarkers.

This request is exempt from the Office of Management and Budget's review under 5 CFR 1320.3(h)(4): Facts or opinions submitted in response to general solicitations of comments from the public, published in the Federal Register or other publications, regardless of the form or format thereof, provided that no person is required to supply specific information pertaining to the commenter, other than that necessary for self-identification, as a condition of the Agency's full consideration of the comment.

Dated: February 5, 2015.

Leslie Kux,

Associate Commissioner for Policy.

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